

# **REDUCTION IN THE RISK OF HEART FAILURE EVENTS WITH PREVENTIVE CARDIAC RESYNCHRONIZATION THERAPY: The MADIT-CRT Trial**

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for the MADIT-CRT Investigators**

**Hot-line Presentation at ESC  
on Sept. 1, 2009**

**Supported by a research grant from Boston Scientific Co.  
All devices used were from Boston Scientific.**

# DISCLOSURE INFORMATION

Arthur J. Moss, MD

## Company

Boston Scientific Co.

## Relationship

Research Grant  
to Univ. Rochester

Hold no stock or stock options in any device company.  
Not a member of any corporate advisory group or  
speakers' bureau.

# MADIT-CRT (2004-2009)

**Primary Hypothesis:** in minimally symptomatic cardiac pts. with IHD (NYHA I or II) or NIHD (NYHA II), wide QRS ( $\geq 0.13s$ ), and low EF ( $\leq 0.30$ ), CRT-D will reduce the combined end point of all cause mortality or HF event, whichever ever comes first, when compared to ICD-only therapy.

We anticipated that the benefit from CRT-D would be dominated by reduction in HF events.

# MADIT-CRT: Primary End Point

## First Occurrence\*

All-cause Mortality, or

Heart-failure event with S & S of HF with response to Rx:

- 1) iv decongestive therapy in an “out-patient” setting; or
- 2) augmented decongestive iv or oral therapy during in-hospital stay

\*Adjudicated by Independent Blinded End-point Review Committees

# MADIT-CRT: Plan (Achieved)

Enrollment: 1820 pts **(1820)\***

125 enroll. Cntr. US, Canada, & Europe **(110)**

Recruitment rate: ~ 70 pts/mo **(33 pts/mo)**

Randomization: 3:2 CRT-D to ICD-only **(3:2)**

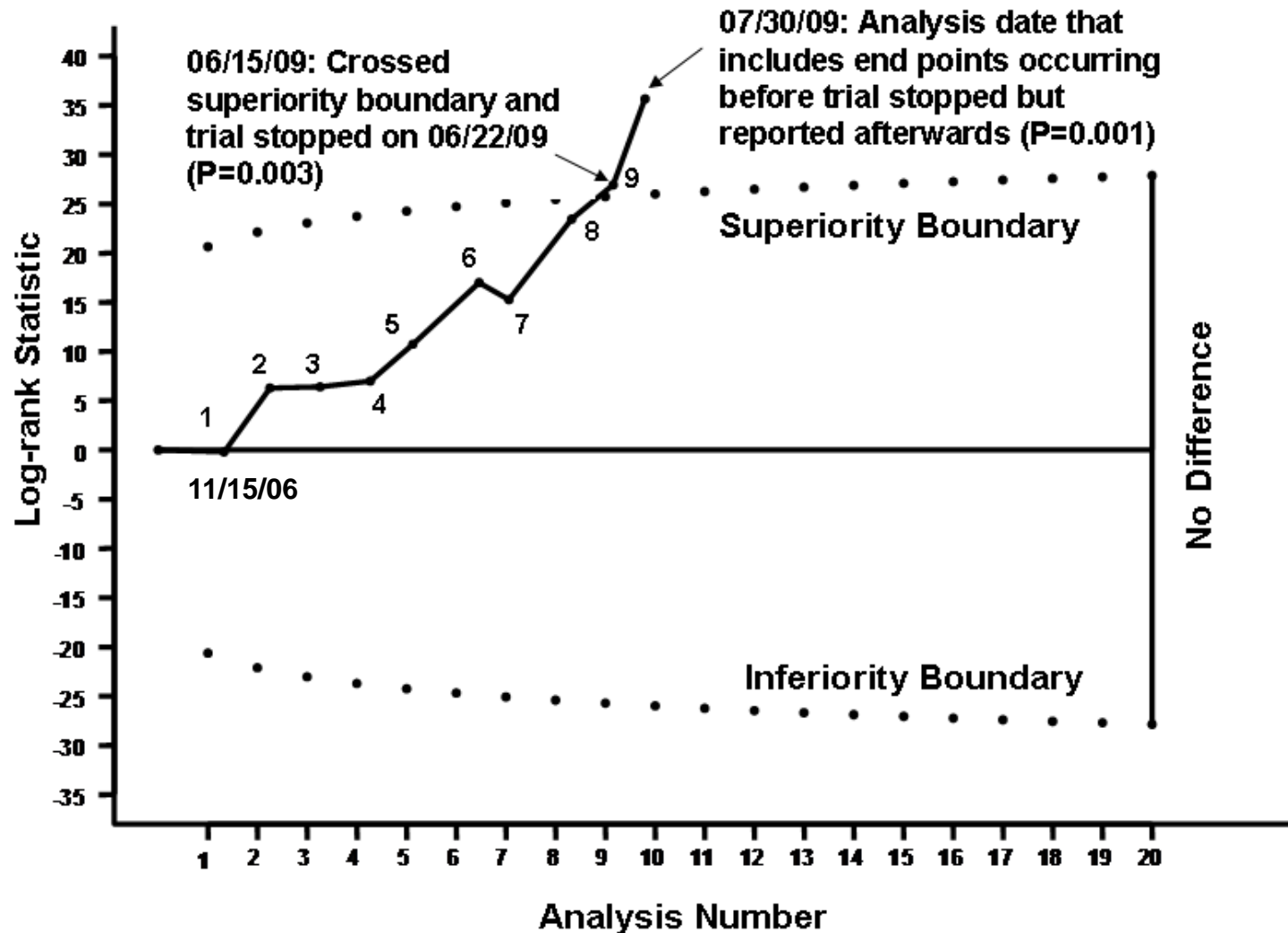
Average follow-up: 24 mo./pt **(29 mo./pt)**

In-hospital heart failure events >80% **(87%)**

Hazard ratio 0.75 **(0.66)**

\*Enrolled patients: US = 1271; Europe = 527; Canada = 22

# Sequential Monitoring in the Group Sequential Design



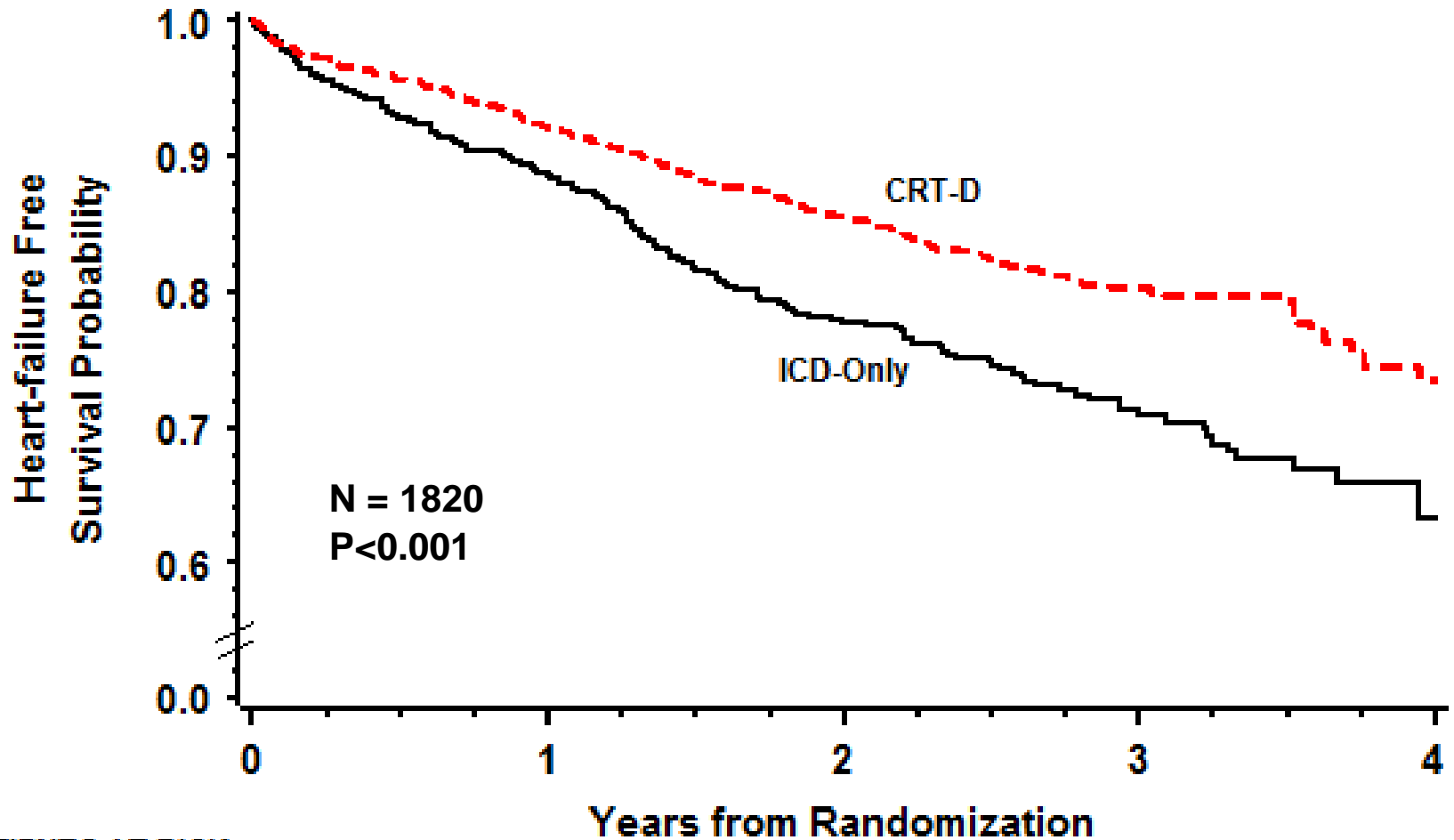
# MADIT-CRT: Baseline Characteristics (percent)

	<u>ICD</u> <u>n=731</u>	<u>CRT-D</u> <u>n=1089</u>
Age $\geq$ 65 yrs	52	54
Male	76	75
IHD	55	55
NYHA Class II	85	86
QRS $\geq$ 150ms	65	64
EF <0.25	53	53
LVEDV >240ml	45	46
LVESV >170ml	45	45

# MADIT-CRT: Baseline Medications (percent)

	<u>ICD</u> <u>n=731</u>	<u>CRT-D</u> <u>n=1089</u>
<b>ACE inhibitors</b>	<b>77</b>	<b>77</b>
<b>ARB</b>	<b>20</b>	<b>21</b>
<b>Beta-blockers</b>	<b>93</b>	<b>93</b>
<b>Diuretics</b>	<b>73</b>	<b>76</b>
<b>Statins</b>	<b>67</b>	<b>67</b>

# MADIT-CRT: Kaplan-Meier Estimate of Heart-failure Free Survival Probability



## PATIENTS AT RISK

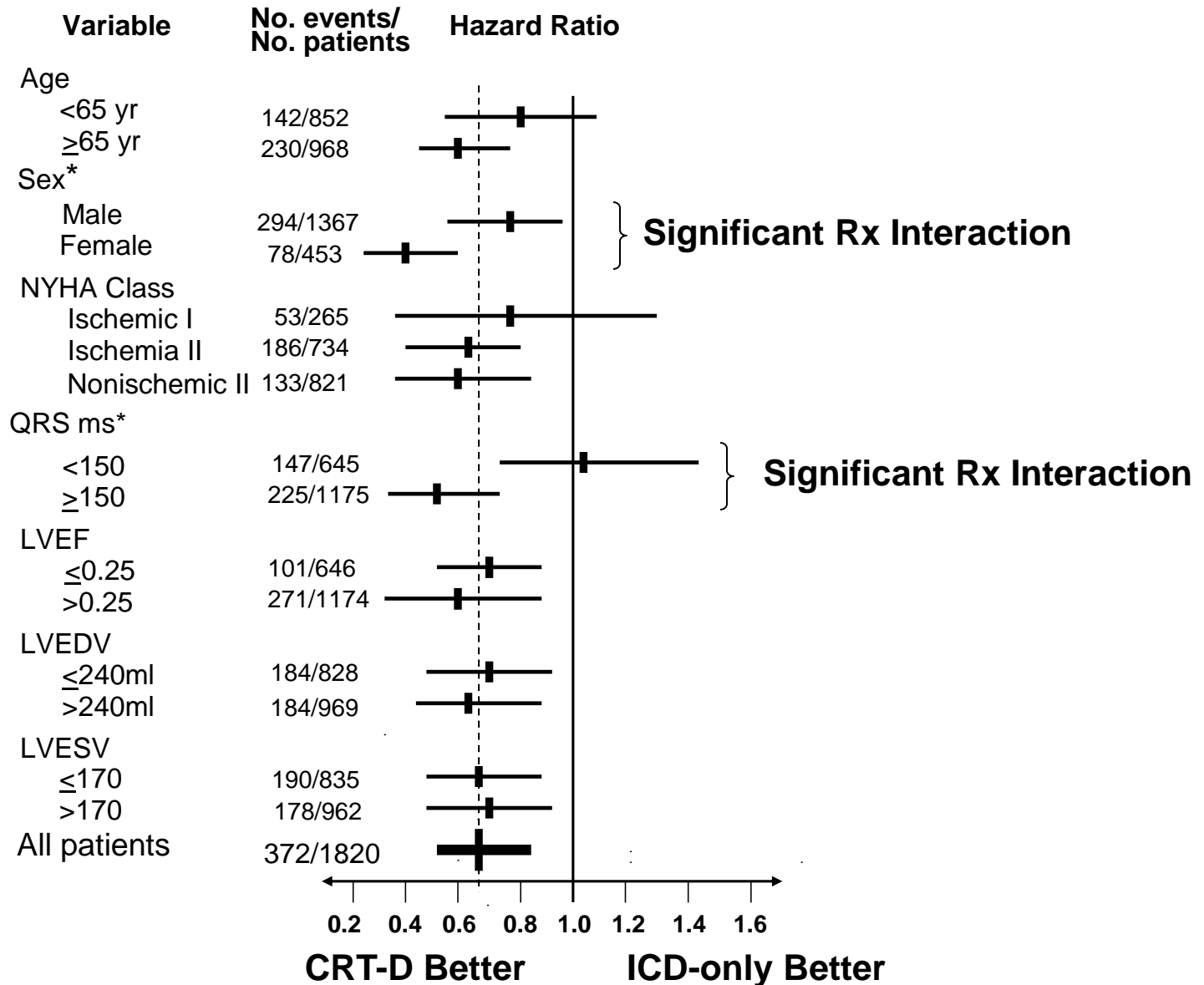
	0	1	2	3	4
ICD-Only	731	621 (0.89)	379 (0.78)	173 (0.71)	43 (0.63)
CRT-D	1089	985 (0.92)	651 (0.86)	279 (0.80)	58 (0.73)

# MADIT-CRT: Cox Analyses

Patients (#ICD;#CRT)	End Point		Hazard Ratio (95% CI)	P-Value
	ICD # events	CRT [%]		
<b>All Patients*</b> (731; 1089)	<b>Death/HF</b>		<b>0.66</b> (0.52-0.84)	<b>0.001</b>
	185 [25.3]	187 [17.2]		
	<b>Heart Failure</b>		<b>0.59</b>	<b>&lt;0.001</b>
	167 [22.8]	151 [13.9]		
	<b>Death (any time)</b>		<b>1.00</b>	<b>0.99</b>
	53 [7.3]	74 [6.8]		

\*Prespecified primary analysis.

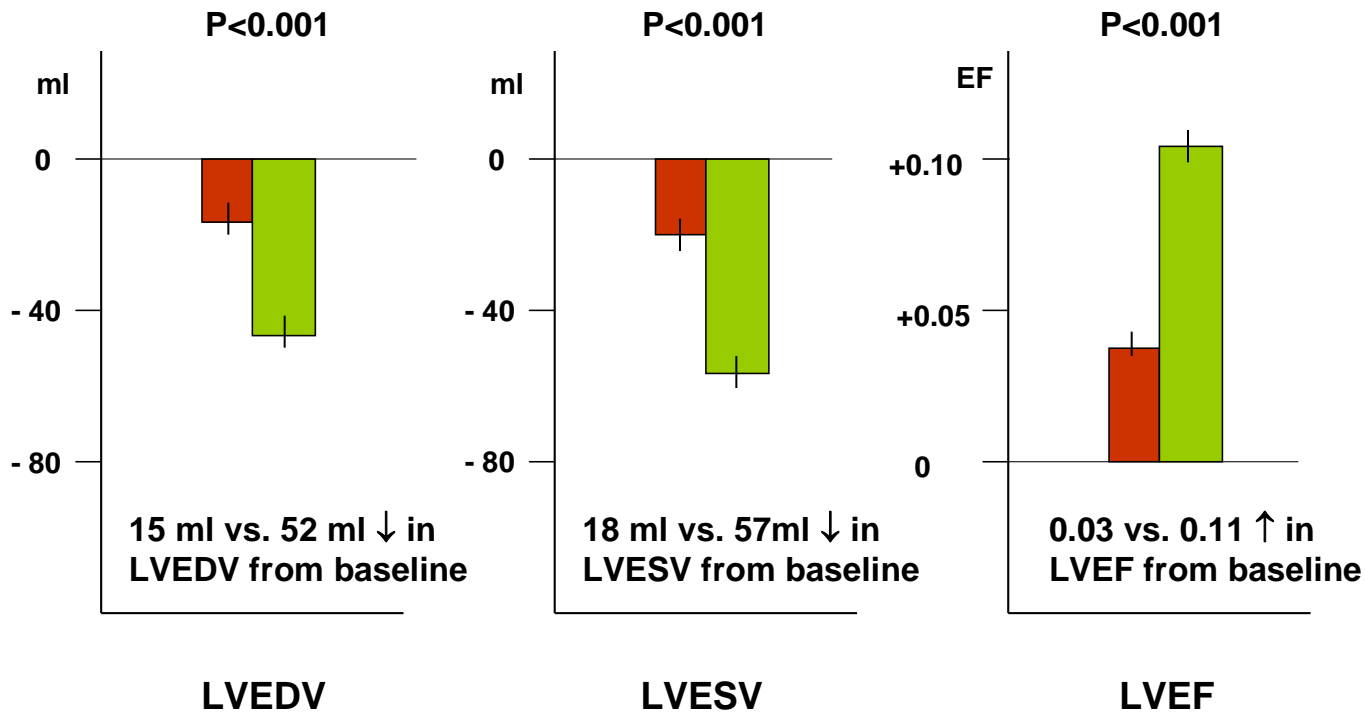
# CRT-D:ICD Hazard Ratios for Prespecified Subgroups



# Mean Changes in Echo LV Volumes and EF from Baseline to 1-year by Treatment Group

N=620  
ICD-only

N=746  
CRT-D



# MADIT-CRT: Conclusions

- CRT-D is associated with a 34% reduction in the risk of death or heart failure events in asymptomatic or mildly symptomatic patients with ischemic or non-ischemic cardiomyopathy ( $\downarrow$ EF and  $\uparrow$ QRS)
- CRT-D benefit is driven by a 41% reduction in the risk of first HF events
- CRT therapy is more effective in women than men, and in patients with wider than narrower QRS complexes
- CRT-D is effective in preventing heart failure in mildly symptomatic at-risk cardiac patients

# **MADIT-CRT Executive Committee**

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**James Daubert, MD (Rochester & Durham)**

**Mark Estes, MD (Boston)**

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**THANK YOU**